

Hyperandrogenism of Tumor Origin in Adolescence: A Case Report

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Abstract

A case is presented of hyperandrogenism with signs of virilization in an adolescent female. The symptoms include deepening of the voice, marked acne on the face and upper back, increased hair in the genital area and buttocks, and amenorrhoea of two months' duration. The patient was diagnosed with ovarian Sertoli-Leydig cell tumor on the basis of blood tests, gynaecological ultrasound and magnetic resonance imaging. She underwent laparoscopic unilateral adnexectomy, with immediate normalization of the laboratory test findings and progressive clinical improvement following surgery.

Keywords: Hyperandrogenism; Amenorrhoea; Magnetic Resonance Imaging (MRI); Laparoscopic Unilateral Adnexectomy

Introduction

Sertoli-Leydig cell tumour is a rare disorder in clinical practice [1]. It is included among ovarian stromal tumours (5% of all ovarian tumours) and accounts for approximately 0.2-0.5% of all ovarian neoplasms [1,2].

This type of tumour is characterised by the presence of sex cord-derived cells (Sertoli cells) and stromal-derived cells (Leydig cells and fibroblasts), in variable proportions within the same tumour [3], and can occur at any time of life, but is most common in women under 40 years of age (75% of all cases).

They usually present with increased androgen production, the most frequent finding being elevated plasma testosterone,

with clinical manifestations including signs and symptoms of virilisation, menstrual disorders in the form of chronic anovulation and infertility [4].

Surgical removal of the tumour usually results in normalisation of laboratory test parameters and restoration of feminine characteristics [5].

Case Report

A 12-year-old girl presented with deepening and cracking of the voice, marked acne on the face and upper part of the dorsal region, increased body hair predominantly in the genital zone and buttocks, and the absence of menstruation over the last two months.

Her previous pubertal development had been normal, with menarche in October 2021, and no sexual intercourse. In view of the clinical picture, Pediatrics requested blood testing that revealed increased concentrations of 17-hydroxy-progesterone (7.03 ng/ml), testosterone (3.35 ng/ml) and androstenedione (6.04 ng/ml). An adrenocorticotrophic hormone (ACTH) test to assess a possible adrenal gland origin of the hyperandrogenism proved negative. Abdominal ultrasound in turn revealed a normal left ovary and uterus; the right ovary could not be visualized.

In view of the above findings, the patient was referred to Gynecology and a magnetic resonance imaging (MRI) study was carried out. The gynecological exploration showed a clear increase in body hair in the region of the midline *linea alba*, external genitals and perineal region, together with hypertrophy of the clitoris.

Transrectal ultrasound showed an uterus of normal size and with a thin endometrium. The left ovary was increased in size at the expense of a solid-cystic tumor mass with a low-intensity Doppler signal (Figure 1). The right ovary appeared normal (Figure 2).

Figure 1: Ultrasound view of the left ovary, enlarged in relation to the right ovary and containing solid and cystic areas.

Figure 2: Ultrasound view of the right ovary, of normal dimensions.

Based on the abovementioned ultrasound, clinical and laboratory test findings, a left ovarian Sertoli-Leydig cell tumor was suspected as the cause of hyperandrogenism and secondary virilization of the patient.

The MRI findings were consistent with the suspected diagnosis and showed an enlarged left ovary due to the presence of a tumor mass (4.8 x 3.6 x 3.7 cm). The lesion was well delimited, with a smooth surface and a heterogeneous internal signal intensity showing irregular cystic areas measuring up to 2.2 cm in size and a low signal intensity solid component suggestive of a fibrous stromal mass.

The tumor marker tests proved normal, and a thoracic-abdominal-pelvic computed tomography scan discarded locoregional as well as distant tumor spread. After evaluation of the case by Pediatric Oncology, surgical treatment was decided.

The advisability of left oophorectomy versus laparoscopic left adnexectomy was commented with Pathology, and following a review of the literature on the subject and in order to allow a better analysis of tumor spread, unilateral adnexectomy was decided.

Surgery revealed a normal uterus. Both ovaries were oval in shape, with a smooth pearly surface, and the left ovary was larger than the right ovary (approximate maximum diameter 5 cm and 3 cm, respectively). Both fallopian tubes appeared normal. The rest of the abdominal cavity showed no alterations (Figure 3).

Figure 3: Laparoscopic view showing a uterus of normal appearance and size. Enlarged left ovary with a smooth and pearly surface.

The histopathological study of the surgical piece confirmed the diagnosis of moderate histological grade (G2)(WHO classification) ovarian Sertoli-Leydig cell tumor. The pathological classification (pTNM, AJCC 8th ed.) corresponded to pT1a (FIGO IA): tumor limited to the ovary and with an intact capsule. Disease-free surgical margins and fallopian tube.

With the results obtained, the case was discussed by the Pediatric Oncology Committee of the corresponding reference hospital, and the decision was made to not indicate adjuvant therapy. Controls were therefore scheduled in the outpatient clinic. The patient presented immediate normalization of the laboratory test findings and progressive improvement of the signs of virilization following surgery.

Discussion

Sertoli-Leydig cell tumor (androblastoma or arrhenoblastoma) is an uncommon disorder in clinical practice [1] - hence the importance of reporting cases such as that described in this study.

These tumors may manifest at any point in life, but are more common in women under 40 years of age (75% of all cases), as in our patient. The lesions are typically unilateral, with bilateral presentations accounting for only 5% of all cases [4].

Sertoli-Leydig cell tumors are characterized by increased androgen production, with the most common finding being

plasma testosterone elevation (at least 2.5 times the upper limit of normal). Most lesions are hormonally active (70-85%). The clinical manifestations include signs and symptoms of virilization, such as a deepened voice, anomalous body hair distribution, hirsutism, a hypertrophic clitoris, and menstrual disorders in the form of chronic anovulation, as in our patient, and infertility [4].

Surgical removal of the tumor usually results in normalization of the laboratory test parameters and the restoration of female characteristics [5].

The main prognostic factor is disease stage at the time of diagnosis [6]. Fortunately, the great majority of these tumors (92%) are confined to the ovary (stage I) and present a good prognosis. This allows for conservative management (unilateral adnexectomy), with the preservation of future fertility [4]. In elderly women hysterectomy and bilateral adnexectomy are indicated [3]. Between 3-20% of all cases are diagnosed in advanced stages, with pelvic and abdominal (but not distant) spread [4], requiring pelvic radiotherapy and chemotherapy [3].

In addition to disease stage at the time of diagnosis, other important prognostic factors are patient age and the histological differentiation grade of the tumor [6]. Adequate tumor typing by the pathologist is therefore crucial.

In our case, since the tumor was confined to the ovary (stage I) and exhibited moderate differentiation (G2), management was limited to surgery, with no need for adjuvant therapy.

The 5-year survival rate is 70-90%. Recurrence is infrequent, typically occurs early (within less than 3-5 years), and has a poor prognosis [3]. Close patient monitoring is therefore required during the first years after treatment.

Conclusion

In women, the ovaries and adrenal glands are the main producers of the body's testosterone [6]. Therefore, in a case of hyperandrogenism, a differential diagnosis must be made between the possible ovarian or adrenal origin of the excess androgen production [1].

Sertoli-Leydig cell tumour is a rare entity, accounting for approximately 0.2 to 0.5% of all ovarian tumours [1,2], yet it is the most common androgen-functioning tumour [6].

It can occur at any stage of life, but is most common in women under 40 years of age [4].

Most of them are diagnosed at stage I, with a good prognosis, and surgery is the treatment of choice (unilateral adnexectomy in women with reproductive desire, and hysterectomy and bilateral adnexectomy in older women with no or fulfilled reproductive desire), with regular clinical and analytical follow-up [4].

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